Chapter 10

Case studies using the M- and LM-samplers

10.1 Background to a study

Much of the material in sections 10.1 to 10.5 has recently been published (Thompson, 2000*a*). It was presented at a one-day Royal Statistical Society conference in March 1999, and was discussed again in July 1999 at the CBMS Summer Course. Section 10.6 is the result of more recent work.

First, the methods of the previous chapters are illustrated using data based on an extended Icelandic pedigree, provided by Dr. J. H. Edwards. The trait, apparent in three families, was thought to be a simple recessive, with an animal analogue suggesting a possible location on human Chromosome 1 (Remmers et al., 1996). However, findings were negative, and for purposes of illustration Heath and Thompson (1997) simulated marker data, conditional on a recessive trait locus in the chromosomal region. The resimulation of data assumed the same marker locations, population allele frequencies, and marker phenotype availability as in the original data. Marker data were simulated conditional on descent paths at the trait locus that implied that the four affected final individuals would be so. No phenotypic assumptions were imposed for other pedigree members. Using these simulated data, there was some evidence for excess gene identity by descent among the six parents of affected individuals (Heath and Thompson, 1997). However, in attempting to analyze these simulated data, under the assumption of a rare recessive trait, findings were ambiguous, primarily due to the fact that no founders were ancestral to more than three of the six parents of the affected individuals, even though the ancestry of the families was fully traced for seven generations. Accounting for the affected individuals required three separate origins of the recessive disease allele within the pedigree. For current purposes, we have therefore also modified the pedigree structure, making possible a single ancestral origin of the disease allele, and realized disease ancestry accordingly (Figure 10.1).

Conditional on the realized gene ancestry, we have resimulated marker data.